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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/516,492

01/27/2006

Kenneth Kinzler

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EXAMINER

CHUNDURU, SURYAPRABHA

ART UNIT

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1637

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/516,492	<b>Applicant(s)</b> KINZLER ET AL.	
	<b>Examiner</b> Suryaprabha Chunduru	<b>Art Unit</b> 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 24 May 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-4,7,9-32 and 34-36 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4,7,9-32 and 34-36 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 December 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

**DETAILED ACTION**

1. The Applicants' response to the office action filed on May 24, 2008 has been considered and acknowledged.

***Status of the Application***

2. Claims 1-4, 7, 9-32, 34-36 are pending. Claims 5-6, 8, 33 were cancelled. New claim 36 is added. All arguments and amendment have been fully considered and deemed persuasive in part for the reasons that follow. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. The action is made FINAL necessitated by Amendment.

***New Grounds of rejections necessitated by the Amendment***

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Griseri et al. (European J Human Genetics, Vol. 8, pp. 721-724, 2000) in view of Horikawa et al. (US 6,235,481).

Griseri et al. teach a method of associating a genotype with a phenotype comprising (i) determining levels of expression of an allele of a gene in a first human population (Italian HSCR (hirschsprung disease) patient population) comprising affected individuals, said affected individuals sharing a phenotype (see page 721, col. 2, paragraph 1, page 722, col. 1, paragraph 1);

(ii) determining levels of expression of the allele of the gene in a second human population comprising control samples (control Italian population) not sharing the phenotype, wherein said affected and control individuals are heterozygous for the gene, and wherein expression of the allele is determined independently of the expression of other alleles of the gene; comparing levels of expression of the allele in the first and second populations (see page 721, col. 2, paragraph 1, page 722, col. 1, paragraph 1, col. 2, paragraphs 1-3 under results section, table 1);

(iii) identifying the allele of the gene as having an association with the phenotype if its expression level differs in a statistically significant manner between the first and second populations (see page 722, col. 2, paragraphs 1-3 under results section);

Griseri et al. also teach reverse transcribing mRNA from an individual and comparing the level of expression of an allele with a second allele (see page 722, col. 1, paragraph 2 under

functional assays section); the association of first and second allele in parent and offspring individuals and the transmission of said alleles (see page 722, paragraphs 1-3 under results section).

However, Griseri et al. did not teach said gene as calpain-10.

Horikawa et al. teach a method for determining or detecting a polymorphism in a calpain-10 encoding nucleic acid and its association with type-2 diabetes mellitus (see col. 2, line 58-67, col. 3, line 1-32).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of detecting allelic expression as disclosed by Griseri et al. with a step of detecting calpain-10 gene variants as taught by Horikawa et al. for the purpose of developing a sensitive method for detecting type II diabetes mellitus. One skilled in the art would be motivated to combine the method as disclosed by Griseri et al. with the calpain-10 of Horikawa et al. because an ordinary artisan would have a reasonable expectation of success that the combination would result in a sensitive method for detecting type 2 diabetes mellitus because Horikawa et al. explicitly taught that the calpain-10 gene variants are indicators of type 2 diabetes mellitus and detecting calpain-10 variants or polymorphisms as an indication of the propensity of type 2 diabetes mellitus (see col. 2, line 58-67) and such modification of the method would be obvious over the cited prior art.

***Response to arguments:***

4. With regard to the objection to the drawings, Applicants' amendment and arguments are fully considered and found persuasive. The objection is withdrawn herein in view of the amendment.

5. With regard to the rejection of claims 1-4, 7, 9-18 under 35 USC 112 first paragraph, Applicants' arguments were fully considered and found persuasive and the rejection is withdrawn herein in view of the persuasive arguments.

6. With regard to the rejection of claims 1, 7, 9, 11-14, 16-18, 34, 35 under 35 USC 102(b) as being anticipated by Egyed et al., Applicants' arguments were fully considered and found unpersuasive. Applicants argue that Egyed et al. does not teach or suggest gene expression products, instead Egyed taught DNA only, based on sequencing and fragment length analysis of alleles and assert the gene expression is not related to DNA analysis and support their arguments based on the dictionary meaning for gene expression. Applicants' arguments are found unpersuasive. First, Examiner notes that instant claims recite allele expression, which clearly indicate the expression at DNA level and not at the RNA or protein level as asserted by the Applicants. Further the dependent claims recite determination of allelic expression based on determining sequence variation by single-base extension or use of dye terminators and detection of the expression of alleles by capillary electrophoresis - which clearly read on the DNA expression. Thus the instant claims as presented do not exclude allelic expression at DNA level. Applicants also argue that Egyed only teaches gene frequencies and does not teach levels or amounts of gene expression. Applicants' arguments were found unpersuasive because the gene frequencies represent quantitative analysis and thus the number relates to the amount of allelic expression. Further the claims as presented do not require gene expression; rather the claims recite expression of an allele of a gene, which clearly read on DNA. Thus the limitations upon which the arguments were based are not present in the claims and as noted in MPEP 2145 Although the claims are interpreted in light of the specification, limitations from the specification

are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). As discussed in the rejection *Egyed et al.* does teach the expression of an allele of a gene and therefore *Egyed et al.* does anticipate the instant claims. Accordingly the rejection is maintained herein.

7. With regard to the rejection of claims 1-2, 7, 11-13, 15-17 under 35 USC 102(b) as being anticipated by *Sieber et al.*, Applicants' arguments were fully considered and found unpersuasive. As discussed above Applicants' arguments based on gene expression were found unpersuasive since the expression of an allele of a gene does correlate with DNA and the dependent claims further support the expression of an allele at DNA level. The limitation 'level of expression (RNA or protein)' upon which the arguments were based, are not present in the claims and as noted MPEP 2145 Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

8. With regard to the rejection of claims 1-4, 7, 10-13, 16, 18 under 35 USC 102(b) as being anticipated by *Griseri et al.*, Applicants' arguments were fully considered and found unpersuasive. Applicants argue that the like *Sieber* and *Egyed*, *Griseri et al.* does not teach gene expression, instead, *Griseri et al.* teach SNP variants determined by exon trapping experiments. As discussed above Applicants' arguments based on gene expression were found unpersuasive since the expression of an allele of a gene based on SNP variants does correlate with DNA and the dependent claims. The limitation 'level of expression (RNA or protein)' upon which the arguments were based, are not present in the claims and as noted MPEP 2145 Although the

claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

9. With regard to the rejection of claims 19-32 under 35 USC 103(a) as being obvious over Griseri in view of Yoshikawa, Applicants' arguments are fully considered and found unpersuasive. Applicants argue that there is no teaching or suggestion to combine the cited references, as Griseri et al. does not teach comparing the level of expression of an allele with a second allele and Yoshikawa does not remedy the deficiencies of the primary reference. Applicants' arguments are found unpersuasive. First, as discussed above the instant claims do not exclude the teachings of Griseri et al.. Second, Griseri et al. does teach expression of an allele in the disease condition and compared it with the expression of the allele in a control sample. Third, the instant claims do not require the expression of an allele at RNA or protein level, instead the claims as presented encompass allelic expression at DNA level. Fourth, examiner notes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in thereferences themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992). In the instant context, the ordinary artisan would have had a reasonable expectation of success that the combination of the method with the differential labeling of Yoshikawa would result in a sensitive and improved method as discussed in the rejection. Accordingly the rejection is maintained.

### ***Conclusion***

No claims are allowable.



Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Suryaprabha Chunduru/

Primary Examiner, Art Unit 1637